including Attachment 3. (C)

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| 60/236,370 | 29 September 2000 (29.09.2000) | US |
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| 60/237,038 | 2 October 2000 (02.10.2000) | US |
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*[Continued on next page]*

(54) Title: NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES

(57) Abstract: The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

WO 2001/055326 A3

# NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES

Claims of **WO0155326**

Translate this text

What Is Claimed Is :
1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consistingof :
(a) a polynucleotide fragmentof SEQ ID NO : X or a polynucleotide fragment of the cDNA sequence contained in Clone ID NO : Z, which is hybridizable to SEQ ID NO : X ;
(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO : Y or a polypeptide fragment encoded by the cDNA sequence contained in cDNA Clone ID NO : Z, which is hybridizable to SEQ ID NO : X ;
(c)a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO : X or a polypeptide fragment encoded by the cDNA sequence contained in cDNA Clone ID NO : Z, which is hybridizable to SEQ ID NO : X ;
(d) a polynucleotide encoding a polypeptide domain of SEQ ID NO : Y or a polypeptide domain encoded by the cDNA sequence contained in cDNA Clone ID NO : Z, which is hybridizable to SEQ ID NO : X ;
(e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO : Y or a polypeptide epitope encoded by the cDNA sequence contained in cDNA Clone ID NO : Z, which is hybridizable to SEQ ID NO : X ;
(f) a polynucleotide encoding a polypeptide of SEQ ID NO : Y or the cDNA sequence contained in cDNA Clone ID NO : Z, which is hybridizable to SEQ ID NO : X, having biological activity ;
(g) a polynucleotide which is a variant of SEQ ID NO : X ;
(h) a polynucleotide which is an allelic variant of SEQ ID NO : X ;
(i) a polynucleotide which encodes a species homologue of the SEQ ID NO : Y ;
(j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)- (i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO : Y or the polypeptide encoded by the cDNA sequence contained in cDNA Clone ID NO : Z, which is hybridizable to SEQ ID NO : X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO : X or the cDNA sequence contained in cDNA Clone ID NO : Z, which is hybridizable to SEQ ID NO : X.

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the Nterminus.

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the Nterminus.

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.

11. An isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence selected from the group consistingof :
(a) a polypeptide fragment of SEQ ID NO : Y or the encoded sequence contained in cDNA Clone ID NO : Z ;
(b) a polypeptide fragment of SEQ ID NO : Y or the encoded sequence contained in cDNA Clone ID NO : Z, having biological activity ;
(c) a polypeptide domain of SEQ ID NO : Y or the encoded sequence contained in cDNA Clone ID NO : Z ;
(d) a polypeptide epitope of SEQ ID NO : Y or the encoded sequence contained in cDNA Clone ID NO : Z ;
(e) a full length protein of SEQ ID NO : Y or the encoded sequence contained in cDNA Clone ID NO : Z ;

(f) a variant of SEQ ID NO : Y ;
(g) an allelic variant of SEQ ID NO : Y ; or
(h) a species homologue of the SEQ ID NO : Y.

12. The isolated polypeptide of claim11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim11.

14. A recombinant host cell that expresses the isolated polypeptide of claim11.

15. A method of making an isolated polypeptide comprising :
(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed ; and
(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polynucleotide of claim1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising :
(a) determining the presence or absence of a mutation in the polynucleotide of claim 1 ; and
(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising :
(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample ; and
(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
(a) contacting the polypeptide of claim 11 with a binding partner ; and
(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO : Y.

22. A method of identifying an activity in a biological assay, wherein the method comprises :
(a) expressing SEQ ID NO : X in a cell ;
(b) isolating the supernatant ;
(c) detecting an activity in a biological assay ; and identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

24. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim11.

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Attachment 3.

<!--StartFragment-->AAS33284/c

ID  AAS33284 standard; cDNA; 2547 BP.

XX

AC  AAS33284;

XX

DT  04-DEC-2001  (first entry)

XX

DE  DNA encoding human secreted protein, Seq ID No 243.

XX

KW  Immunomodulatory; human immunodeficiency virus; HIV; anaemia; angina;
KW  rheumatoid arthritis; antiarteriosclerotic; cardiant; vascular;
KW  cerebroprotective; thrombolytic; antimicrobial; ophthalmological;
KW  cytostatic; Alzheimer's disease; Parkinson's disease; human; cancer;
KW  multiple sclerosis; cancer; hyperproliferative disorder; infection;
KW  Gaucher's disease; neurological disease; cerebrovascular disorder;
KW  thrombosis; wound healing; ss.

XX

OS  Homo sapiens.

XX

PN  WO200155326-A2.

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PD  02-AUG-2001.

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PF  17-JAN-2001; 2001WO-US001347.

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PR  31-JAN-2000; 2000US-0179065P.
PR  04-FEB-2000; 2000US-0180628P.
PR  24-FEB-2000; 2000US-0184664P.
PR  02-MAR-2000; 2000US-0186350P.
PR  16-MAR-2000; 2000US-0189874P.
PR  17-MAR-2000; 2000US-0190076P.
PR  18-APR-2000; 2000US-0198123P.
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PR 08-DEC-2000; 2000US-0251990P.
PR 11-DEC-2000; 2000US-0254097P.
PR 05-JAN-2001; 2001US-0259678P.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
XX
PI Rosen CA, Barash SC, Ruben SM;
XX
DR WPI; 2001-451931/48.
DR P-PSDB; AAU20575.
XX
PT New nucleic acids and polypeptides, useful for diagnosing, preventing or
PT treating medical conditions.
XX
PS Claim 1; SEQ ID NO 243; 753pp; English.
XX
CC The invention relates to novel isolated nucleic acid molecules (I)
CC encoding human secreted proteins (II). (I) and (II) are used to prevent,
CC treat or ameliorate a medical condition in e.g. humans, mice, rabbits,
CC goats, horses, cats, dogs, chickens or sheep. (I) and (II) may be used in
CC the prevention, treatment and diagnosis of diseases associated with
CC inappropriate expression of secreted proteins. (I) and complementary
CC sequences may also be used as DNA probes in diagnostic assays (e.g.
CC polymerase chain reactions (PCR)) to detect and quantitate the presence
CC of similar nucleic acid sequences in samples, and so which patients may
CC be in need of restorative therapy. (II) may also be used as antigens in
CC the production of antibodies and in assays to identify modulators
CC (agonists and antagonists) of the expression and activity of the secreted
CC proteins. The anti-(II) antibodies and antagonists may also be used to
CC down regulate expression and activity of (II). The anti-(II) antibodies
CC may also be used as diagnostic agents for detecting the presence of (II)
CC in samples (e.g. by enzyme linked immunosorbant assay (ELISA)). The
CC disorders include for example: immune/autoimmune diseases (e.g. HIV
CC (human immunodeficiency virus) infections, anaemia, rheumatoid arthritis
CC and multiple sclerosis), cancers and hyperproliferative disorders (e.g.
CC melanomas, neoplasms of the breast or liver, Sezary syndrome and
CC Gaucher's disease), neurological diseases (e.g. Alzheimer's disease,
CC Parkinson's disease and Charcot-Marie-Tooth disease), cardio-/

CC cerebrovascular disorders (e.g. cardiac arrest, tachycardia, angina and
CC thrombosis), infections caused by bacteria, viruses and fungi and ocular
CC disorders (e.g. corneal infections). (I) and (II), agonists, antagonists
CC and antibodies can also be used to promote wound healing, maintain organs
CC before transplantation, and support cell culture of primary tissues.

Query Match 23.9%; Score 343.2; DB 4; Length 2547;
Best Local Similarity 78.4%; Pred. No. 3.1e-97;
Matches 411; Conservative 0; Mismatches 113; Indels 0; Gaps 0;

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Qy       912 AATTTGGATTAGAATCTTCTGAAACTGCTAATTTTACAGGCTTTTCTTACAGACATCCTA 971
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Db      2547 AATTTGGATTAACATCTTTAGGAAACACGAGTTTTACAGACTTTTCTTGCAAACATCCTA 2488

Qy       972 GAGAGCATCGAGCAAAAGCCCCTGCAACGCAGCCCAGGGTTCACTCTGAAGCCAGAGCTC 1031
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Db      2487 GAGAACTGCGAGAAAAGATTCCTGTTAAGCAGCCCAGGATCTGCTCTGAAACCAGGTCTC 2428

Qy      1032 TCAATGAGCATTTTTTGAGCGTGGATGCGTTCGACAGTCAGATTGTAGAGTCACAGGTAG 1091
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Db      2247 AAGTAAGAAAAAATTTTCAAAAGACGTGGCAGGAGAGTGGAAGAGTTTTTAAAGGCCTGG 2188

Qy      1272 GATATGAAACCTCGGATGCACATGCGACAGAAATGAGCAGGGCCTTCCAGGAGGAATTGG 1331
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Db      2187 GATATGCAACCGCAGATGCTTCTGCAACTGAGATGAGAACCACCTTCCAAGAGGAATCTG 2128

Qy      1332 CCTTTTTGAGTGAAACTGTTGGTCCAAGACAAGGAAATCTGCATAATTTGTCAAAAGACG 1391
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Db      2127 CATTTATAAGTGAAGCTGCTGCTCCAAGACAAGGAAATATGTATACTTTGTCAAAAGACA 2068

Qy      1392 GTTTATCCAATGGAGTGCCTCGTAGCAGACCAGCAGAATTTTCA 1435
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<!--EndFragment-->